Melanotan II — Basic Review Questions

1. What is Melanotan II, what type of peptide is it, and what is its regulatory status?

Answer: Melanotan II (MT-II) is a synthetic, NON-selective melanocortin receptor agonist — a cyclic analogue of α-MSH (a cyclic heptapeptide, ~1024 Da, engineered to be superpotent and degradation-resistant). The crucial features are that it activates several melanocortin receptors at once and that it crosses the blood–brain barrier. It is NOT approved for human use anywhere: the FDA issued a warning letter in 2007, with parallel warnings from European, Australian, and Irish regulators, and there are no completed Phase 3 trials. It exists only as a research / grey-market peptide, given by subcutaneous injection with no approved formulation.

2. How does Melanotan II work?

Answer: Its tanning comes from the same pathway as Melanotan I — it binds MC1R on melanocytes, raises cAMP, and drives MITF and eumelanin synthesis. But because MT-II is non-selective, it also activates MC3R (energy), MC4R (appetite and sexual function), and MC5R (exocrine glands), and it reaches the brain. That broad, central activation is exactly why it produces so much more than a tan: MC4R in the brain drives erections and appetite suppression, MC3R/MC4R affect autonomic and cardiovascular tone, and MC5R touches sebaceous glands. The single most important concept is that there is no way to isolate the tan — the same molecule that darkens skin necessarily produces the sexual, appetite, nausea, flushing, and blood-pressure effects.

3. What is Melanotan II used for, and how strong is that evidence?

Answer: People use it (off-label, unapproved) for rapid cosmetic tanning, and secondarily for sexual stimulation and appetite/metabolic effects. The human evidence is real but very thin: pigmentation was shown in a 3-subject Phase I pilot, and erectile response in roughly 80–85% of men across two small trials (n=10 and n=20). Everything else — the metabolic, neuroprotective, and immune-modulating effects — is animal or in-vitro data. There are no large or long-term human trials and no completed Phase 3 studies for any indication, so its efficacy claims rest on a handful of subjects plus mechanism.

4. How does Melanotan II differ from Melanotan I (and from PT-141)?

Answer: MT-II and MT-I share the same MC1R pigmentation engine but otherwise diverge sharply. Melanotan I is linear, MC1R-selective, does not meaningfully cross the blood–brain barrier, and is FDA/EMA-approved (Scenesse, for the light-sensitivity disorder EPP) — so it gives a “clean” tan and photoprotection without sexual or appetite effects. Melanotan II is cyclic, non-selective across MC1/3/4/5R, does cross into the brain, and is approved nowhere — so it tans faster and more potently but adds central sexual and appetite effects and a much broader side-effect profile. The clinical lesson is comparative: most single effects people want from MT-II are delivered more safely by an approved drug — Melanotan I for photoprotection, and PT-141 (Vyleesi), an MC3R/MC4R agonist, for sexual desire (HSDD). MT-II's niche is essentially “everything at once,” which is rarely what a patient actually needs.

5. What are the main concerns or dangers with Melanotan II?

Answer: There are three layers of concern. First, the unregulated product itself — grey-market peptides of unknown purity, frequently mislabeled (MT-I sold as MT-II and vice versa) and contaminated — is often a bigger hazard than the pharmacology, which is why regulators on three continents have issued warnings. Second, melanoma: MT-II darkens existing moles, and case reports link it (often alongside sunbed use) to melanoma; no causal link is proven, and in-vitro data are paradoxically anti-tumor, but the signal demands caution because users tend to chase more sun with less sunscreen, and MC1R variants independently raise risk. Third, specific dangerous interactions: do NOT combine it with PDE5 inhibitors (sildenafil/tadalafil) because of priapism risk; avoid it around skin procedures (laser, microneedling, peels, tattoos) because of hypersensitivity reactions with marked hyperpigmentation; and use extreme caution in hypertension, since MC4R-driven sympathetic output can transiently raise blood pressure.

6. What are the key contraindications and monitoring requirements, and what is the main limitation to remember?

Answer: Contraindications include a personal or family history of melanoma or other skin cancer, concurrent PDE5 inhibitor use (priapism), pregnancy and lactation, and concurrent sunbed use; skin procedures should be kept completely separate. Monitoring is non-negotiable: a baseline full-body skin exam with dermoscopy and nevus photography, then skin/nevi surveillance every 3–6 months (biopsy any changing lesion), blood-pressure checks at each visit and in the first two hours after the first dose, and periodic bloodwork with continued use. If priapism (an erection lasting over 4 hours) occurs, discontinue immediately. The key limitation to remember: Melanotan II is unapproved everywhere, its human evidence is tiny, and its non-selectivity makes side effects inseparable from the tan — so where a specific effect is the goal, an approved, quality-controlled alternative (Melanotan I or PT-141) is almost always the better choice.